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Docket No.: C1041.70005US00
(PATENT)

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant:	Hermann Wagner et al.
Serial No.:	09/355254
Confirmation No.:	6183
Filed:	February 22, 2000
Patent No.:	7001890
For:	PHARMACEUTICAL COMPOSITIONS COMPRISING A POLYNUCLEOTIDE AND OPTIONALLY AN ANTIGEN ESPECIALLY FOR VACCINATION

Examiner:	J. J. Zara
Art Unit:	1635

Certificate of Mailing Under 37 CFR 1.8(a)

I hereby certify that this paper (along with any paper referred to as being attached or enclosed) is being deposited with the U.S. Postal Service on the date shown below with sufficient postage as First Class Mail, in an envelope addressed to: Attention: Certificate of Correction Branch, Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.

Dated: March 1, 2006

Alan W. Steele, M.D., Ph.D., Registration No. 45,128

REQUEST FOR CERTIFICATE OF CORRECTION PURSUANT TO 37 CFR 1.322

Attention: Certificate of Correction Branch
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Dear Sir:

Upon reviewing the above-identified patent, Patentee noted the following typographical errors, which should be corrected.

1. In the Specification, in the middle of page 21, and in the patent, column 12, beginning at line 43, Table 2 and the two paragraphs following Table 2 are missing and should appear, as follows:

Table 2 Sequences of oligomers and death due to lethal shock

a		
1668	TCCAT**GACGTT**CCTGATGCT	(SEQ ID NO: 4)
CRE	ATTGCCT**GACGTCA**GAGAGC	(SEQ ID NO: 5)
1668-CA	TCCAT**GACGTC*A***CTGATGCT	(SEQ ID NO: 6)
CRE-TC	*ATTGCCT***GACGTT*C*GAGAGC**	(SEQ ID NO: 7)
b		
1668	5/5	
CRE	0/5	
1668-CA	0/3	
CRE-TC	3/3	

Lethality was determined as in Example 2. The 1668 sequence fortuitously contains a combination of transcription response elements, namely the transcription factor binding sites (TGACGTTCC). This element represents the binding site for HSVIP04 (ATF), HSINS04 (CREB half site), CAMV35SR03 (HBP-1a yeast) or ADE422 (AP-1) in combination with an HSIL606 site which is a repressor site (sequence analysis from EMBL database Heidelberg). This sequence can be found in the 5' non-coding regions (promoters) of several eukaryotic cytokine genes including human IL-13 promoter and IL-12 p40 intron 1. The CRE sequence contains all the response elements cited above except for HSIL606 and it contains the full CRE palindromic sequence (TGACGTCA). In accordance with the invention, the CRE sequence did not induce death and changes in the 1668 eliminate toxicity.

TNF-α release is a hallmark of lethal toxic shock [Tracey, K. J. et al., Science 234, 470-474 (1986), Tracey, K. J. et al., Nature 330, 662-664 (1987)]. An exchange of only two nucleotides between CRE and 1668 resulted in a loss of macrophage induced TNF-α release activity. The sequence of the corresponding oligonucleotide is given in Table 2. The reported 6-mer active core sequence of 1668 contains the CpG flanked by two 5' purines and two 3' pyrimidines. The exchange of CA for TC does not affect this motif, however, TNF-α release was severely diminished. Thus, the broader core 8-mer sequence or the transcription response element and not the surrounding sequence environment was responsible for these effects. In accordance with the invention, when utilizing macrophage derived TNF-α release as a marker, the information comprised in the prior art 5'Pu-Pu-CpG-Py-Py-3' motif alone was not satisfactory for predicting oligomer activity or toxicity. Additionally, in contrast to 1668, CRE did not induce IL-6 release in vivo or from the ANA-1 cell line in vitro.

2. In the Specification, at the top of page 25, and in the patent at column 13, line 49, in the title of Table 4, "Sequence of ukary tic TRE te t d" should read: --Sequences of eukaryotic TRE tested--.

3. In the Specification, in the middle of Table 4 on page 25, and in the patent at column 13, line 58, in Table 4, "STAT 4 CTGATTTCCCCGAAATGATG (SEQ ID NO: 19)" should read: --STAT 4 CTGATTTCCCCGAAATGATG (SEQ ID NO: 19)--.

These errors were not in the application as filed or amended by Patentee; accordingly no fee is required.

Transmitted herewith is a proposed Certificate of Correction effecting such amendments. Patentee respectfully solicits the granting of the requested Certificate of Correction.

Respectfully submitted,
Hermann Wagner et al., Patentee

By _____

Alan W. Steele, M.D., Ph.D.
Registration No.: 45,128
WOLF, GREENFIELD & SACKS, P.C.
Federal Reserve Plaza
600 Atlantic Avenue
Boston, Massachusetts 02210-2206
(617) 646-8000

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UNITED STATES PATENT AND TRADEMARK OFFICE
CERTIFICATE OF CORRECTION

PATENT NO. : 7001890

APPLICATION NO. : 09/355254

ISSUE DATE : February 21, 2006

INVENTOR(S) : Hermann Wagner et al.

It is certified that an error appears or errors appear in the above-identified patent and that said Letters Patent is hereby corrected as shown below:

At column 12, beginning at line 43, please insert the following:

Table 2 Sequences of oligomers and death due to lethal shock

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1668	TCCAT**GACGTT**CCTGATGCT	(SEQ ID NO: 4)
CRE	ATTGCCT**GACGTC**AGAGAGC	(SEQ ID NO: 5)
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b

1668	5/5
CRE	0/5
1668-CA	0/3
CRE-TC	3/3

(Continued on next page)

MAILING ADDRESS OF SENDER
Alan W. Steele, M.D., Ph.D.
WOLF, GREENFIELD & SACKS, P.C.
Federal Reserve Plaza
600 Atlantic Avenue
Boston, Massachusetts 02210-2206

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